A Phase I Dose-Escalation Study of Human GM-CSF Gene-Transduced Irradiated Allogeneic Prostate Cancer Cell Vaccine (GVAX®) Prostate Cancer Vaccine [PC-3]) in Patients with Hormone-Refractory Prostate Cancer

Nontechnical Abstract

Prostate cancer is a common form of cancer in adult males in the US. In 1997, 32,891 men died from prostate cancer in the United States. Surgical removal of the prostate or radiation treatment may cure early prostate cancer if the tumor has not spread outside the prostate gland. However, in 70% of patients, the cancer will spread, mostly to the bone. At this point, the cancer cannot be cured. Hormone therapy can control advanced cancer temporarily in most patients, but the advanced cancer progresses in nearly all patients. Once a patient's cancer no longer responds to hormone therapy, chemotherapy may relieve pain or other symptoms caused by the tumors, but there is no treatment that can improve survival.

GVAX® Prostate Cancer Vaccine (PC-3) is a vaccine made from cells taken from the tumor of a patient with advanced prostate cancer. To make the vaccine, the cells are altered by inserting a gene for GM-CSF, (granulocyte-macrophage colony-stimulating factor), a substance made by the body that helps the immune system recognize a tumor and destroy it. The gene for GM-CSF is inserted into the prostate cancer cells using an artificial virus containing parts of a natural virus called "Adeno-associated Virus." The cells are then grown in a laboratory to produce the vaccine. The vaccine cells are treated with radiation so they cannot grow or divide after injection. The cells themselves are not radioactive. The cells are frozen to preserve them until they are administered to the patient.

This is an exploratory Phase I clinical trial. The primary objective is to observe adverse events, ie, anything unusual that happens, in patients receiving three different doses of GVAX® Prostate Cancer Vaccine (PC-3), in order to determine a dose to use in Phase II trials. The secondary objectives are (1) to observe any antitumor or therapeutic response as measured by lowering of prostate specific antigen (PSA) levels in the blood, the length of time a patient experiences improvement or stabilization of his condition and how long the patient survives, and (2) to measure serum GM-CSF levels in the blood after each vaccination as an indirect measure of how the vaccine cells are functioning.

Subjects in the study must have histologically diagnosed adenocarcinoma of the prostate and must no longer respond to hormone therapy. Subjects who have received radiation treatments to more than 25% of their bone marrow (or any radiation within 6 months of the first vaccination) are not eligible for this trial. Patients who have received prior gene therapy, chemotherapy, biologic therapy, or immunotherapy also are not eligible for enrollment in this trial.

Nine to 15 subjects will be entered into the study in groups of three and will receive three doses of GVAX® Prostate Cancer Vaccine (PC-3), one about every 28 days. Each dose level will consist of injections into the skin as follows: Dose Level 1, 50 million cells per dose producing GM-CSF of approximately 85 μg per 24 hours and a total number of cells in all three doses of 150 million; Dose Level 2, 100 million cells per dose producing GM-

CSF of approximately 170 μg per 24 hours and a total number of cells in all three doses of 300 million; Dose Level 3, 200 million cells per dose producing GM-CSF of approximately 340 μg per 24 hours and a total number of cells in all three doses 600 million.

Patients will be followed for one year after they start receiving treatment. Assessments include observation of subjects for adverse events, any new cancer, and any new diagnoses of autoimmune disease.